Attorney Docket No. 21486-032 DIV1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT :	Wands et al.		
SERIAL NUMBER :	09/903,023	EXAMINER :	Yu, Misook
FILING DATE :	July 11, 2001	ART UNIT :	1642
FOR :	DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS		

August 7, 2002
Boston, Massachusetts

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF MICHAEL S. LEBOWITZ UNDER 37 C.F.R. §1.132

I, Michael S. Lebowitz, declare and state as follows:

1. I am employed by Panacea Pharmaceuticals, Inc., licensee of the technology claimed by the patent application referenced above. I am a principal investigator on projects involving neurodegenerative disorders and cancer.

2. I received a B.S. degree from the Brandeis University in 1989 and a Ph D. in Biological Chemistry from The Johns Hopkins University School of Medicine in 1995.

3. I have read the Office Action mailed on February 7, 2002 and am familiar with the Examiner's grounds of rejection of the pending claims.

4. Experiments were carried out to measure the level of HAAH in normal and cancer tissues and bodily fluids. The assays were carried out as described on page 14-15 of the specification of the present patent application The experiments described in this declaration were carried out under my direction.

5. Bodily fluid samples were collected from normal (no known cancer) individuals as well as individuals diagnosed with breast or prostate cancers. Detection of HAAH was accomplished using a sandwich ELISA which was developed using HAAH-specific antibodies, FB50 and 5C7. The data indicate that an increase in the level of HAAH polypeptide in a human bodily fluid as measured using an HAAH-specific antibody (compared to normal control levels) correlates with the presence of a malignant neoplasm. Results are listed in Table 1, below.

Table 1: Detection of HAAH in Serum

Serum Source (total # samples)	*# samples*	*Level of HAAH*
Normal Control (16)	14	-
	1	+/-
	1	+
Breast Carcinoma (12)	3	-
	2	+/-
	7	+
Prostate Cancer (5)	0	-
	0	+/-
	5	+

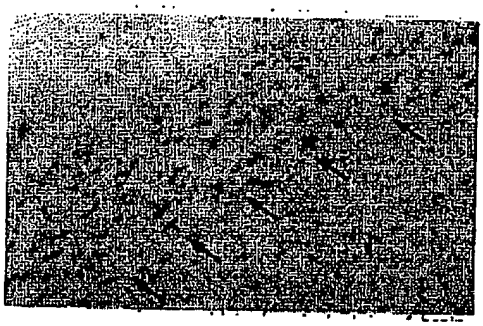
6. Tissue samples were collected from normal (no known cancer) individuals as well as individuals diagnosed with a variety of different cancers. Detection of HAAH was accomplished by immunostaining with HAAH-specific antibodies FB50 and 5C7. HAAH levels

were found to be increased in all cancer types studied to date compared to normal control tissues. HAAH was over-expressed in 99% of all tumor samples tested vs. 0% of control samples. Normal control tissues included tissue samples from individuals with no known cancer as well as normal noncancerous tissue adjacent to a tumor. The data indicate that an increase in HAAH in a tissue sample correlates with a diagnosis of a malignant neoplasm. Results are shown in Table 2, below.

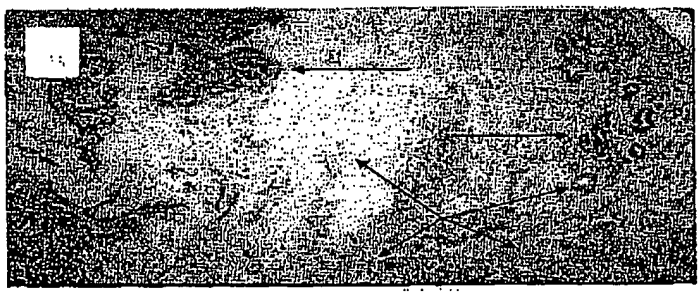
Table 2: Immunostaining of primary human tumor biopsy specimens

Tumor tissue	HAAH+/Total
Cholangiocarcinoma	120/120
Intrahepatic cholangiocarcinoma	48/50
Prostate cancer	3/3
Breast cancer	7/7
Pancreatic cancer	37/37
Glioblastoma	24/25
Oligodendroglioma	8/9
Primitive neuroectodermal	12/12
Colon cancer	150/150
Ovarian cancer	17/17
Total	426/430

7. Immunohistochemical staining of patient-derived tissue sections revealed intense staining in regions of a tumor mass and minimal or no staining of adjacent normal tissue. For example, Fig. 1 (shown below) showed immunohistochemical staining of brain tissue from a glioblastoma patient. Patches of dark staining indicate presence of HAAH in tumor tissue; intense staining was detected at the tumor periphery.



Figs. 2 shows immunohistochemical staining of a tissue sample containing a pancreatic carcinoma. Fig. 2 shows intense staining of bulk tumor (left, horizontal arrow) and neoplastic ducts (right, horizontal arrow), and minimal or no staining of surrounding parenchyma, normal ducts, and adjacent normal tissue (diagonal arrows).



8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that

these statements were made with the knowledge that willful false statements and the like so made are punishable by a fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date 8/7/02

Michael S. Lebowitz, Ph.D.